UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

D8/949,904

APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/949,904	10/15/97	LAVALLIE E	GI-5288B

EXAMINER	
UNGAR, S	
ART UNIT	PAPER NUMBER
1642	12

HM22/0427

STEVEN R LAZAR
GENETICS INSTITUTE INC
87 CAMBRIDGE PARK DR
CAMBRIDGE MA 02140

DATE MAILED: 04/27/99

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on August 19, 1998 & January 29, 1999

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 18, 19, 20, 22, 23, 25, 28, 29 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☑ Claim(s) 29 is/are allowed.
☑ Claim(s) 18, 19, 20, 22, 23, 25, 28 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☑ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

1. The Amendment filed November 23, 1998 (Paper No. 9) in response to the Office Action of August 19, 1998 (Paper No. 9) and the Amendment filed January 29, 1999 (Paper No. 11) in response to the Letter of January 19, 1999 (Paper No. 10) are acknowledged and have been entered. Previously pending claims 1-7, 21, 24, 26 and 27 have been canceled, claims 18 and 20 have been amended and new claims 28 and 29 have been added. Claims 18-20, 22, 23, 28 and 29 are currently being examined.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The following rejections are being maintained:

Claim Rejections - 35 USC § 112

4. Claim 20 remains rejected under 35 USC 112 for the reasons previously set forth in Paper No. 8, Section 3, pages 3-5.

Applicant argues that (a) the Federal Circuit Court of Appeals has specified that the PTO should accept the truthfulness of tstatements in the disclosure in the absence of sound reasoning and that the specification contains disclosure of *in vivo* utility supported by an experimental demonstration of related *in vitro* utility, (b) the specification provides sufficient guidance to predict the efficacy of the claimed therapeutic compositions with a reasonable expectation of success and there is nothing in the record to establish that undue experimentation is required to determine the optimal dosage or mode of administration, (c) Examiner's arguments are speculative and there is no support for Examiner's suspicion that such disadvantages actually exist.The argument has been noted but has not been found

persuasive because (a) the sound scientific reasoning presented in the rejection is both recognized and well understood by those of skill in the art. For example, Freshney (Culture of Animal Cells, A Manual of Basic Technique, Alan R. Liss, Inc., 1983, New York, p4) teach that it is recognized in the art that there are many differences between cultured cells and their counterparts *in vivo*. These differences stem from the dissociation of cells from a three-dimensional geometry and their propagation on a two-dimensional substrate. Specific cell interactions characteristic of histology of the tissue are lost. The culture environment lacks the input of the nervous and endocrine systems involved in homeostatic regulation in vivo. Without this control, cellular metabolism may be more constant *in vitro* but may not be truly representative of the tissue from which the cells were derived. This has often led to tissue culture being regarded in a rather skeptical light (p. 4, see Major Differences *In Vitro*). Further, although drawn to *in vitro* assays for cancer therapy and their correlation to *in vivo* therapeutic efficacy, Dermer (Bio/Technology, 1994, 12:320) is clearly applicable to the understanding of the correlation between *in vitro* assays and *in vivo* therapeutic efficacy of the instant invention, especially in view of the teaching on page 19 of the specification that the composition may have prophylactic use in the prevention of pancreatic tumors. Dermer teaches that, "petri dish cancer" is a poor representation of malignancy, with characteristics profoundly different from the human disease Further, Dermer teaches that when a normal or malignant body cell adapts to immortal life in culture, it takes an evolutionary-type step that enables the new line to thrive in its artificial environment. This step transforms a cell from one that is stable and differentiated to one that is not, yet normal or malignant

cells *in vivo* are not like that. The reference states that evidence of the contradictions between life on the bottom of a lab dish and in the body has been in the scientific literature for more than 30 years. Clearly it is well known in the art that cells in culture exhibit characteristics different from those *in vivo* and cannot duplicate the complex conditions of the *in vivo* environment involved in host-tumor and cell-cell interactions. Thus, based on the cell culture data presented in the specification, it could not be predicted that, in the *in vivo* environment, the claimed composition would have therapeutic effects or that a therapeutic amount could be formulated, (b) the disclosure of therapeutic effects, in the absence of working examples is not sufficient to predict the efficacy of the claimed therapeutic compositions with a reasonable expectation of success for the reasons disclosed above in section (a), (c) it is clear that Examiner's arguments were based on sound scientific reasoning that is conventionally understood and well known by those of skill in the art as exemplified by the cited references above. Applicant's arguments have not been found persuasive and the rejection is maintained.

Double Patenting

5. Claims 18-20, 22, 23 and 25 remain provisionally rejected under the judicially created doctrine of double patenting over claims 18-20, 22, 23 and 25 of copending Application No. 08/848,439 for the reasons previously disclosed in Paper No. 8, Section 6, pages 5-6.

Applicant argues that they elected claims directed to SEQ ID Nos 1 and 2 and related materials in the copending application so that claims pertaining to polypeptides and compositions are not being examined in that application, nor have

any of the claims been allowed. The argument has been noted but has not been found persuasive because the claims in the copending application have not been canceled. Further, claim 19 is drawn to culturing a DNA molecule comprising nucleotides 316-1143 of SEQ ID NO:1. If the copending claims 18-20, 22, 23 and 25 were to canceled, a provisional obviousness-type double patenting rejection would be imposed because it would be obvious to transform a cell with SEQ ID NO:1 to produce SEQ ID NO:2. Applicant's arguments have not been found persuasive and the rejection is maintained.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

6. Claim 29 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claim is drawn to a pharmaceutical composition comprising a protein comprising the amino acid sequence from amino acids 21 to 295 of SEQ ID NO:2.

Inherent to pharmaceutical compositions is an *in vivo* use thereof. The specification does not provide guidance by way of general methods or working examples which teach the feasibility of *in vivo* use of the claimed composition. The claim is rejected for the reasons previously set forth in Paper No. 8, Section 4, pages 3-5, drawn to claim 20. The arguments drawn to the rejection of claim 20 are relevant to the instant rejection. The arguments have been noted but have not been found persuasive for the reasons set forth above.

7. All other objections and rejections recited in Paper No. 8 are withdrawn.

8. Claim 29 appears to be free of the art and allowable.

9. Applicant's amendment necessitated the new grounds of rejection.

Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (703) 305-2181. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, can be reached at (703) 308-4310. The fax phone number for this Art Unit is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1640.

Susan Ungar
April 20, 1999

PAULA K. HUTZELL
SUPERVISORY PATENT EXAMINER